UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,245	11/10/2003	Yuan-Tsong Chen	16743-003001 / 12A-920716	3196

26181 7590 03/02/2006

FISH & RICHARDSON P.C.
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
WONG, JENNIFER SHIN SHIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/705,245	CHEN ET AL.	
	Examiner	Art Unit	
	Jennifer Wong	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *November 11, 2003*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-25* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-12, drawn to methods to assess adverse drug reactions by assaying for an allele, classified in class 435, subclass 6.

   II. Claims 13-19, drawn to methods to develop therapies for a cutaneous adverse reaction, classified in class 435, subclass 4.

   III. Claims 20-25, drawn to methods of pharmacogenetic profiling, classified in class 435, subclass 6.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are drawn to patentably distinct methods, requiring different process steps, involving the use of different reagents and /or having different objectives. The methods of invention I require the use of nucleic acid probes or primers, and involves performing hybridization or sequencing steps in order to accomplish the objective of detecting an allele as a means to determine adverse drug reactions. The methods of invention II also require the use of cells, medicines, and performing assay methods to accomplish the objective of developing therapies for adverse drug reactions induced by drugs by assaying for alleles that are indicative of an adverse drug reaction. The methods of invention I and II are novel and unobvious over one another.

Inventions I and III are drawn to patentably distinct methods, requiring different process steps, involving the use of different reagents and /or having different objectives. The methods of invention I require the use of nucleic acid probes or primers, and involves performing hybridization or sequencing steps in order to accomplish the objective of detecting an allele as a means to determine adverse drug reactions. The methods of invention III, require nucleic acid probes or primers, and involve performing hybridization or sequencing steps in order to accomplish the objective of pharmacogentic profiling patients by assaying for HLA-B alleles and genetic factors of thiopurine methyltransferase and genes for the long-QT syndrome. The methods of inventions I and III are novel and unobvious over one another.

Inventions II and III are drawn to patentably distinct methods, requiring different process steps, involving the use of different reagents and /or having different objectives. The methods of invention II also require the use of cells, medicines, and performing assay methods to accomplish the objective of developing therapies for adverse drug reactions induced by drugs by assaying for alleles that are indicative of an adverse drug reaction. The methods of invention III, require nucleic acid probes or primers, and involve performing hybridization or sequencing steps in order to accomplish the objective of pharmacogentic profiling by assaying for HLA-B alleles and genetic factors of thiopurine methyltransferase and genes for the long-QT syndrome. The methods of inventions I and III are novel and unobvious over one another.

3. Further, should Applicants elect invention I, it is subject to a further restriction as follows.

The claims have been presented in improper Markush format, as distinct products and distinct methods are improperly joined by the claims. Invention I reads on patentably distinct inventions drawn to multiple HLA-B alleles. The claims encompass HLA-B*1502, HLA-B*5801, and HLA-*4601. These alleles consist of distinct nucleotide sequences, and a further restriction is applied to each invention. Applicants must elect a single HLA-B allele to be examined.

It is noted that each of the HLA-B alleles constitute distinct chemical compounds and each has a distinct functional property. The chemical structure of each HLA-B alleles and of each molecule of a HLA-B allele is distinct from each of the other HLA-B alleles. For example, a HLA-B*1502 allele chemically, structurally and functionally distinct from HLA-B*5801. Further, a search for a HLA-B*1502 would not be co-extensive with a search for HLA-B*5801. Additionally, a reference which renders obvious a HLA-B allele will not necessarily also render obvious another HLA-B allele. Similarly, a search indicating that a particular HLA-B allele is novel or unobvious would not extend to a holding that a single polymorphism or a different HLA-B is also unobvious.

Accordingly, HLA-B*1502, HLA-B*5801, and HLA-*4601 alleles are thus deemed to constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such allele is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35

U.S.C. 121 and 37 CFR 1.14. Applicant is advised that this is a restriction requirement and should **not** be construed as an election of species.

Further, should Applicants elect invention I, it is subject to an additional restriction as follows.

Claims 2-4 are subject to an additional restriction since these claims are not considered to recite a proper genus/Markush group.

Specifically, claims 2-4 claim distinct sets of drugs. Each of these drugs consist of distinct chemical, structural and metabolic activity thereby having different biological functions. Given the differences in structure and function, the Markush group set forth in claims 2-4 is not considered to constitute a proper genus, and therefore is subject to a further restriction requirement. A keyword and patent search of these sequences would not be co-extensive with one another. For example, a search for the carbamazepine would not be co-extensive with allopurinol. Further, a reference which renders obvious or non-novel carbamazepine would not also necessarily render obvious or non-novel the allopurinol. Similarly, a finding that carbamazepine is nonobvious or novel does not coextend to a finding that allopurinol is also nonobvious or novel.

Accordingly, a search of more than one of the drugs claims 2-4 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and the corresponding examination of more than one of the claimed sequences. Accordingly, Applicants are required to elect one drug. Note that this is not a species election.

Claims 1, 5-12 link the HLA-B alleles, drug, and adverse drug reactions, each allele, drug, and adverse drug reaction as outlined above. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s). Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.0.

With respect to claim 12, it is subject to a further restriction as follows.

The claim have been presented in improper Markush format, as distinct products and distinct methods are improperly joined by the claims. Invention I reads on patentably distinct inventions drawn to multiple genetic markers. The claims encompass HLA-DRB*1202, Cw*0801, Cw*0806, A*1101, MICA*019, and Cw*0302. These genetic markers consist of distinct nucleotide sequences, and a further restriction is applied to each invention. Applicants must elect a single genetic marker to be examined.

It is noted that each of the genetic markers constitute distinct chemical compounds and each has a distinct functional property. The chemical structure of each genetic marker and of each molecule of the genetic markers is distinct from each of the other genetic marker. For example, HLA-DRB*1202 is chemically, structurally and functionally distinct from Cw*0801. Further, a search for HLA-DRB*1202 would not be co-extensive with a search for Cw*0801. Additionally, a reference which renders obvious HLA-DRB*1202 will not necessarily also render obvious Cw*0801. Similarly, a search indicating that HLA-DRB*1202 is novel or unobvious would not extend to a holding that a Cw*0801 is also unobvious.

Accordingly, HLA-DRB*1202, Cw*0801, Cw*0806, A*1101, MICA*019, and Cw*0302 genetic markers are thus deemed to constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such genetic marker is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.14. Applicant is advised that this is a restriction requirement and should **not** be construed as an election of species.

In summary, should invention I be elected, Applicant is required to elect one HLA-B allele, one drug, and one genetic factor.

6. Further, should Applicants elect invention II, it is subject to an additional restriction as follows.

The claims have been presented in improper Markush format, as distinct products and distinct methods are improperly joined by the claims. Invention II reads on patentably distinct inventions drawn to multiple HLA-B alleles. The claims encompass HLA-B*1502, HLA-B*5801, and HLA-*4601. These alleles consist of distinct nucleotide sequences, and a further restriction is applied to each invention. Applicants must elect a single (1) allele OR one combination of alleles to be examined.

It is noted that each of the HLA-B alleles constitute distinct chemical compounds and each has a distinct functional property. The chemical structure of each HLA-B alleles and of each molecule of a HLA-B allele is distinct from each of the other HLA-B alleles. For example, HLA-B*1502 and HLA*4601 alleles chemically, structurally and functionally distinct from HLA-B*5801. Further, a search for a HLA-B*1502 and HLA*4601 would not be co-extensive with a search for HLA-B*5801. Additionally, a reference which renders obvious a HLA-B allele will not necessarily also render obvious another HLA-B allele. Similarly, a search indicating that a particular HLA-B allele is novel or unobvious would not extend to a holding that a single polymorphism or a different HLA-B is also unobvious.

Accordingly, HLA-B*1502, HLA-B*5801, and HLA-*4601 alleles and combinations thereof are thus deemed to constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such allele is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.14. Applicant is advised that this is a restriction requirement and should **not** be construed as an election of species.

7. Further, should Applicants elect invention II, this group is subject to an additional restriction requirement as follows

Claims 15-18 are subject to an additional restriction since these claims are not considered to recite a proper genus/Markush group.

Specifically, claims 15-18 claim distinct sets of adverse drug reactions, drugs, and HLA-B alleles consisting of Stevens-Johnson syndrome or toxic epidermal necrolysis, carbamazepine, and HLA-B*1502; and, Stevens-Johnson syndrome or toxic epidermal necrolysis, allopurinol, and HLA-B*5801. Each of these drug reactions, drugs, and alleles consist of distinct chemical and physiological responses; chemical, structural and metabolic activity; and molecular, chemical, physical, and nucleotide sequences respectively, thereby having different biological functions. Given the differences in structure and function, the Markush group set forth in claims 15-18 is not considered to constitute a proper genus, and therefore is subject to a further restriction requirement. A keyword and patent search of these sequences would not be co-extensive with one another. For example, a search for the Stevens-Johnson syndrome or toxic epidermal necrolysis, carbamazepine, and HLA-B*1502 would not be co-extensive with Stevens-Johnson syndrome or toxic epidermal necrolysis, allopurinol, and HLA-B*5801. Further, a reference which renders obvious or non-novel Stevens-Johnson syndrome or toxic epidermal necrolysis, carbamazepine, and HLA-B*1502 would not also necessarily render obvious or non-novel the Stevens-Johnson syndrome or toxic epidermal necrolysis, allopurinol, and HLA-B*5801. Similarly, a finding that

Stevens-Johnson syndrome or toxic epidermal necrolysis, carbamazepine, and HLA-B*1502 nonobvious or novel does not coextend to a finding that Stevens-Johnson syndrome or toxic epidermal necrolysis, allopurinol, and HLA-B*5801 is also nonobvious or novel.

Accordingly, a search of more than one of the adverse drug reactions, drugs, and alleles as claimed in claims 15-18 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and the corresponding examination of more than one of the claimed sequences. Accordingly, Applicants are required to elect one drug, HLA-B allele. Note that this is not a species election.

Claims 13, 14, and 19 link the HLA-B alleles, drug, and adverse drug reactions, each allele, drug, and adverse drug reaction as outlined above. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s). Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In*

re Ziegler, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.0.

In summary, should Applicant elect invention II, Applicant is required to elect a either one allele OR one combination of HLA-B alleles; AND one drug.

8. Further, should Applicants elect invention III, it is subject to an additional restriction as follows.

The claims have been presented in improper Markush format, as distinct products and distinct methods are improperly joined by the claims. Invention III reads on patentably distinct inventions drawn to multiple HLA-B alleles. The claims encompass HLA-B*1502, HLA-B*5801, and HLA-*4601. These alleles consist of distinct nucleotide sequences, and a further restriction is applied to each invention. Applicants must elect a one allele OR one combination of alleles to be examined.

It is noted that each of the HLA-B alleles, and combinations thereof, constitute distinct chemical compounds and each has a distinct functional property. The chemical structure of each HLA-B alleles and of each molecule of a HLA-B allele is distinct from each of the other HLA-B alleles. For example, a HLA-B*1502 and HLA-B*4601 allele chemically, structurally and functionally distinct from HLA-B*5801. Further, a search for a HLA-B*1502 and HLA-B*4601 would not be co-extensive with a search for HLA-B*5801. Additionally, a reference which renders obvious a HLA-B allele will not necessarily also render obvious another HLA-B allele. Similarly, a search indicating that

a particular HLA-B allele is novel or unobvious would not extend to a holding that a single polymorphism or a different HLA-B is also unobvious.

Accordingly, HLA-B*1502, HLA-B*5801, and HLA-*4601 alleles are thus deemed to constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such allele is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.14. Applicant is advised that this is a restriction requirement and should **not** be construed as an election of species.

8. These inventions are distinct for the reasons given above and have acquired a different status in the art as demonstrated by their different classification and recognized divergent subject matter. Further, inventions I-IIII require different searches that are not co-extensive. For instance, a patent and keyword search for the methods to assess adverse drug reactions of invention I is not co-extensive with a patent and keyword search for the methods to develop therapies for cutaneous adverse reactions of invention II or the pharmacogenetic profiling methods of invention III. Further, a finding that the method of invention I is anticipated or obvious over the prior art would not necessarily extend to a finding that the methods of inventions II and III were also anticipated or obvious over the prior art. Similarly, a finding that the method of invention I is novel and unobvious over the prior art would not necessarily extend to a finding that the methods of invention II and III are also novel and unobvious over the prior art.

Accordingly, examination of these distinct inventions would pose a serious burden on the examiner and therefore restriction for examination purposes as indicated is proper.

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

10. Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Wong whose telephone number is (571) 272-1120. The examiner can normally be reached on Monday-Friday; 8 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jennifer Wong

CARLA J. MYERS
PRIMARY EXAMINER